

EXHIBIT B

**UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON**

**IN RE: ETHICON, INC., PELVIC
REPAIR SYSTEM PRODUCTS
LIABILITY LITIGATION**

**THIS DOCUMENT RELATES TO
WAVE 4 CASES**

**Master File No. 2:12-MD-02327
MDL 2327**

**JOSEPH R. GOODWIN
U.S. DISTRICT JUDGE**

EXPERT REPORT OF SARAH COLLINS, M.D.

TVT and TVT-Exact

Background and Education

I am a board certified Obstetrician Gynecologist since 2009 with subspecialty certification in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) achieved in 2013. I am currently an Assistant Professor of Obstetrics and Gynecology in the Division of FPMRS at Northwestern Medicine and specialize in treating pelvic floor disorders, including urinary incontinence. After graduating Magna Cum Laude from Cornell University, my medical career began at Wayne State University School of Medicine, where I earned my Doctor of Medicine degree in 2003. I then completed my residency training in obstetrics and gynecology at the Case Western Reserve / MetroHealth / Cleveland Clinic program in 2007. I then completed my FPMRS fellowship training at Hartford Hospital / The University of Connecticut Health Center in 2011. Before accepting my current position at Northwestern Medicine, I was an Assistant Professor of Obstetrics and Gynecology in the Section of Gynecology and Reconstructive Pelvic Surgery at The University of Chicago from the Fall of 2011 through the Spring of 2016.

Since the beginning of my fellowship training, I have published 19 peer-reviewed papers. I also have participated in the peer-review process as a reviewer for journals such as The American Journal of Obstetrics and Gynecology, the International Urogynecology Journal, and Neurourology and Urodynamics. I have worked with residents consistently since my fellowship training, and in my current position, I work with FPMRS fellows as well. I have enjoyed teaching both groups in the operating room, outpatient clinic settings, and as a research mentor. Since I teach residents and fellows, I am very familiar with their baseline knowledge of potential complications that are associated with anti-incontinence surgeries and how to manage those complications, including potential graft complications from midurethral sling repairs. I am also responsible for teaching residents and fellows how to properly counsel patients about potential risks of surgery, proper patient selection, how to avoid surgical complications, how to manage complications of mesh and non-mesh repairs, how to follow-up post-operatively with patients, how to assess graft material properties and clinical outcomes,

the importance of reviewing and interpreting data on the frequency and severity of complications reported in the medical literature, and hands on instruction on proper surgical technique, including but not limited to tension-free placement of midurethral slings such as the TVT. As part of my training and experience, as well as my role in educating residents and fellows and review of various curricula, complications associated with mesh and non-mesh stress urinary incontinence surgeries are well known, including but not limited to dyspareunia, pelvic pain, and voiding difficulties, all of which can be transient or chronic. These are known and accepted risks of any incontinence surgery; however, the safety profile favors midurethral slings compared to native tissue Burch or autologous fascial sling procedures.

I am a member of the American Urogynecologic Society (AUGS), the Society of Gynecologic Surgeons (SGS), the American College of Obstetricians and Gynecologists (ACOG), and the American Association of Gynecologic Laparoscopists (AAGL). Through AUGS, I hold a position on the Clinical Practice Committee, which constructs evidence-based guideline statements on the practice of Female Pelvic Medicine and Reconstructive Surgery (FPMRS). In this role, I contributed to the AUGS Best Practice Statement on the Management of Mesh/Graft Complications in Urogynecologic Surgery document, which will be published soon, by personally writing the portion on midurethral slings. I also serve as the Clinical Practice Committee's Liaison to the Terminology Committee, which strives to standardize the language used in AUGS documents and research endeavors. All of the opinions I have offered in this report are held to a reasonable degree of medical certainty. My Curriculum Vitae is attached as Exhibit 1.

Clinical Experience

My residency training in Obstetrics and Gynecology introduced me to the full breadth of gynecologic surgeries including hysterectomies by every route, hysteroscopy, advanced laparoscopy, surgical emergency operations, and most fortunately, a very in depth exposure to urogynecology. In residency, I performed multiple vaginal hysterectomies with native tissue apical suspensions and anterior and posterior repairs. I also assisted on abdominal and

laparoscopic sacral colpopexy procedures. For urinary incontinence, I performed Burch colposuspensions, as well as transobturator and retropubic midurethral slings. In addition to learning to practice evidence-based medicine, I learned about the inherent risks associated with incontinence surgeries and how to counsel patients on the risks and benefits of these procedures. Although I reviewed the Instructions for Use (IFU) for various midurethral slings, I did not rely on a manufacturer to inform me of the potential risks of incontinence surgery, nor would it be appropriate to rely heavily on an IFU. The risks of incontinence surgeries, including the TVT and midurethral slings, are commonly known to surgeons as they are taught in residency and fellowship programs, reviewed in the medical textbooks and medical literature that surgeons are expected to review, and in presentations at various continuing medical education events, congresses, symposiums, grand rounds, lectures, and various meetings and conferences put on by the professional societies.

During my fellowship I received training in performing pubovaginal slings (also known as autologous fascial slings) and honed my skills in Burch colposuspension and became adept at both procedures. Additionally, I continued to perform hundreds of midurethral slings via retropubic and transobturator approaches, including Ethicon's mechanically cut and laser cut TVT midurethral slings. I was also expected to become familiar with mesh properties and the clinical significance of such properties, such as Amid type 1 macroporous, monofilament, lightweight meshes like TVT compared to a microporous mesh such as Gore-Tex.

Materials Reviewed

Throughout my career, I have extensively researched, reviewed, and contributed to the published medical literature describing the safety and efficacy of TVT and midurethral slings. In addition to reviewing the materials on my reliance list, in preparing this report I have searched and reviewed extensively the medical and scientific literature regarding the design defect allegations as well as searches related to the safety and efficacy of incontinence procedures. I have reviewed the TVT and TVT-Exact Instructions for Use, Patient Brochures, Professional Education videos, slides, and materials. Additionally, I have reviewed plaintiffs' experts' general

reports and the literature and documents they rely upon to support their opinions. A complete list of the materials I have reviewed is attached to my report as Exhibit 2. I reserve the right to amend my report and reliance list as new testimony or materials become available to me.

Fees

My expert fees in this matter are as follows: \$500/hour for reviewing cases, working on reports, and meetings; \$7000/day or \$4000/half-day for a full for deposition testimony and / or trial testimony.

Stress Urinary Incontinence

Stress urinary incontinence (SUI) is the involuntary loss of urine caused by sphincter deficiency and/or urethral hypermobility, typically occurring with exertion such as laughing, coughing, or sneezing. SUI is a very common and debilitating problem affecting about 50% of women at some point in their lives. (Ford 2015 Cochrane Review). Although SUI has a significant impact on the quality of life of women, it is both greatly underestimated and widely untreated, and the majority of women with incontinence tend to be restricted in their social and sexual activities owing to embarrassment and inconvenience. (Wu, 2014). The number of women who underwent inpatient SUI procedures increased from 48,345 in 1979 to 103,467 in 2004, as well as a rapid increase in procedures between 1998 to 2007, which is likely the result of the introduction of the minimally invasive TVT. (Wu, 2011; Anger 2009). The total number of incontinence surgeries in the United States also increased drastically. An estimated 30% of women with SUI in the United States choose to undergo corrective surgery. (Kinchen, 2004). Approximately 13.6% of American women will undergo surgery for stress urinary incontinence by the age of 80, and many of these women will actually endure more than one surgery for this condition. (Wu, 2014). Wu and colleagues put this cumulative risk rate into perspective by noting that “a woman’s lifetime risk of developing breast cancer is 14.8%, whereas the lifetime risk of lung cancer is 6.3%.” They also found peaks in incidence of SUI surgery around age 46 and ages 70-71 years.

Historical treatments for SUI

Before the widespread use of polypropylene midurethral slings, other surgical procedures were commonly performed for the treatment of stress incontinence in women. One such procedure involved suture suspension of the periurethral tissue designed to elevate the bladder neck into the peritoneal cavity. This elevation would then allow increased intra-abdominal pressure to be transmitted to the bladder and proximal urethra equally, maintaining a relationship of higher urethral than bladder pressure, therefore maintaining continence. Urethropexy procedures require abdominal incisions and utilize different fixation points depending on the procedure. In the Marshall Marchetti Kranz (MMK) procedure, the periurethral vaginal tissue is suspended by permanent suture to the periosteum of the superior pubic ramus. In the Burch urethropexy, developed later, the periurethral vaginal tissue is fixed instead to Cooper's ligament¹. The MMK procedure conferred a risk of osteitis pubis, an inflammatory or infectious condition that can develop from the disruption of the integrity of the periosteum with a foreign body². While Burch procedures do not have the same risk of osteitis pubis, like MMK procedures, they require a small low-transverse abdominal incision or laparoscopic incisions.

The urethropexy procedures are associated with some adverse reactions. These include significant post-operative morbidity, an increased occurrence of voiding difficulties, genital prolapse, and recurrent incontinence over time. For example, Alcalay, et al described postoperative de novo detrusor instability on urodynamics in 14.7% of women 3 months after Burch colposuspension³. Kinn⁴ (1995) reported a broad spectrum of late complications including rectocele, cystocele, urge incontinence, cicatricial hernia, and coital pain as well as early complications of ureteric kinking, fascial rupture, pulmonary embolism, hematoma,

¹ Atlas of Pelvic Surgery, On-Line Edition, atlasofpelvicsurgery.com, Wheelless, Clifford R.; Roenneburg, Marcella L. Retropubic Urethropexy: Marshall-Marchetti-Krantz And Burch Operations.

² Lentz SS. Osteitis pubis: a review. Obstet Gynecol Surv. 1995 50(4):310-5

³ Alcalay M, et al. Burch colposuspension: a 10-20 year follow up. BJOG 1995 102:740-45

⁴ Kinn AC. Burch colposuspension for stress urinary incontinence. 5-year results in 153 women. Scand J Urol Nephrol. 1995 29(4): 449-55

wound infection, urinary retention, bacteriuria, and urgency. Using a postal questionnaire of 190 women in Sweden, Kjolhede⁵ reported on complications a median of 14 years after surgery. They included de novo voiding problems in 36% of patients and recurrent UTIs in 16% of patients. In a series of 50 women followed for a mean of 4.5 years, Galloway (1987) reported only 44% of patients were cured and complication free after primary Burch colposuspension, and reported an “unacceptable number of complications in both the short term and longer term,” including persistent incontinence, voiding difficulties, urgency, uterine prolapse, enterocele, dyspareunia, and recurrent incontinence⁶. Lose et al, in a series of 80 patients evaluated before and after Burch colposuspension, reported 25% of patients developed severe voiding difficulties in the immediate postoperative period, and 20% of patients developed late voiding difficulties⁷. Eriksen (1990) reported on a series of 86 women treated with Burch colposuspension for stress incontinence, and only 52% of patients were completely dry and free of complications at 5 year follow-up, with 30% needing further incontinence therapy. He reported several complications in his cohort including detrusor instability and enterocele requiring surgical repair, dyspareunia, and recurrent urinary tract infections⁸. In 1992, Wiskind, et al reported on a retrospective review of 131 women who underwent Burch colposuspension with a single surgeon between 1977 and 1986. He found that 26.7% had required surgery to correct genital prolapse. He noted the reported incidence of enterocele after Burch in the published literature ranges from 3% to 17%.⁹

In one retrospective study of 99 women who underwent the MMK procedure for recurrent stress urinary incontinence, Parnell, et al reported a 12.6 % major complication rate

⁵ Long-term efficacy of Burch colposuspension: a 14-year follow-up study. *Acta Obstet Gynecol Scand* 2005; 84: 767–772

⁶ Galloway NTM, et al. The Complications of Colposuspension. *B J Urology* 1987 60:122-24

⁷ Lose G, et al, Voiding difficulties after colposuspension, *Obstet Gynecol*, 1987 69(1):33-38

⁸ Eriksen BC. Long-term effectiveness of the Burch colposuspension in female urinary stress incontinence. *Acta Obstet Gynecol Scand*. 1990 69(1): 45-5-

⁹ Wiskind AK, et al. The incidence of genital prolapse after the Burch colposuspension. *Am J Obstet Gynecol* 1992 167(2): 399-404

including UTI, wound infection, hernia, dehiscence, osteitis pubis, immediate retention, prolonged retention, frequency/urgency, and fistula.¹⁰

Several studies also call into question the long-term efficacy of colposuspension procedures. Alcalay³ reported a decline in cure rates after Burch colposuspension, down to 69% at 10-20 year follow-up. Alcalay noted flaws with three other contemporary 10 year follow-up studies reporting the success of the Burch colposuspension^{11 12}. Two studies that included women who underwent Burch colposuspension or synthetic midurethral sling at the time of sacral colpopexy produced data suggesting better cure rates of stress urinary incontinence with TVT compared to Burch when combined with this prolapse repair^{13 14}. In a recent textbook chapter, Dr. E.R. Mueller¹⁵ provides an overview of retropubic bladder neck suspension surgeries and notes that “[w]ith the advent of synthetic mid-urethral slings, the retropubic suspensions are often referred to as a procedure of historical interest,” however, noting that there is still a role for this procedure “in the armamentarium of the well-versed pelvic surgeon.”

In addition to colposuspension procedures, suburethral bladder neck slings were also widely utilized before the advent of synthetic midurethral slings. These involved the placement of a graft material into the space dissected between the bladder neck and vagina. They also require a lower abdominal incision and are typically fixed with permanent sutures to the fascia

¹⁰ Parnell JP, et al. Management of recurrent urinary stress incontinence by the Marshall-Marchetti-Krantz vesicourethropexy. J Urol. 1984 132(5): 912-14

³ Alcalay M, et al. Burch colposuspension: a 10-20 year follow up. BJOG 1995 102:740-45

¹¹ Herbertsson G et al. Surgical results and urodynamic studies 10 years after retropubic colpourethrocystopexy. Acta Obstet Gynecol Scand 1993 72(4): 298-301

¹² Feyereisl J, et al. Long-term results after Burch colposuspension. Am J Obstet Gynecol 1994 171(3): 647-52

¹³ Lser DM, et al. Abdominal sacrocolpopexy and urinary incontinence: surgical planning based on urodynamics. Am J Obstet Gynecol 2010 202:375e1-5

¹⁴ Patel M, et al. s Burch or mid-urethral sling better with abdominal sacral colpopexy? Int Urogynecol J (2009) 20:787–790

¹⁵ Mueller ER. Complications of Female Incontinence and Pelvic Reconstructive Surgery. Howard B. Goleman (Editor) 2013 Humana Press, New York. Chapter 10, “Retropubic Bladder Neck Suspensions.”

of the rectus abdominis muscles¹⁶. The graft material used can be synthetic, derived from animal tissue of another species, or more often, composed of the patient's own autologous tissue. In these cases, tissue is typically harvested from the anterior rectus abdominis fascial sheath or from the fascia of the lateral thigh known as the fascia lata. The procedures therefore incur risks associated with potentially foreign graft material or with harvesting tissue from another site to be used beneath the urethra. Risks associated with harvesting fascia from the rectus sheath include ventral hernia and wound site infections. Pain at the site of fascia lata harvesting or more serious wound complications can also result. Even when performed without surgical complications, these procedures commonly cause postoperative voiding dysfunction, often requiring prolonged postoperative catheterization. In one randomized trial of Burch colposuspension versus fascial sling, success rates at 2 years for women who underwent fascial slings were greater than those for women who underwent Burch, but fascial sling patients had higher rates of urinary tract infection, voiding dysfunction, and urgency urinary incontinence¹⁷. Cure rates decreased significantly from 2 to 7 year follow-up, dropping from 42% to 13% in the Burch group and from 52% to 27% in the autologous fascial sling group.¹⁸

McGuire (1978) reported that problems with pubovaginal slings "have included persistent postoperative urinary retention, injury to the bladder or urethra during the operation, erosion of the sling into the urethra or bladder as a late complication, and difficulty in judging sling tension to ensure a satisfactory result."¹⁹ Kaplan (1996) reported on 43 patients who underwent fascial slings and reported an average of 28.4 days lost from work, 84 minute operating time, 3.7 days in the hospital, and 17.4 days of catheterization in this cohort²⁰.

¹⁶ Walters and Karram. *Urogynecology and Reconstructive Pelvic Surgery*, 3rd Edition, 2007, 200-01

¹⁷ Albo ME, Richter HE, Brubaker L, et al. Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. *N Engl J Med* 2007 356(21): 2143-54

¹⁸ Richter HE, Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. *J Uro*, 2012 Vol. 188, 485-489

¹⁹ McGuire EJ. Pubovaginal sling procedure for stress incontinence. *J Urol* 1978 119(1):82-84

²⁰ Kaplan SA, et al. Comparison of Fascial and Vaginal Wall Slings in the Management of Intrinsic Sphincter Deficiency. *Urology* 1996 47: 885-89

While there are no high quality randomized trials comparing fascial slings to synthetic midurethral slings, some studies have compared the 2 procedures. Padmanabhan et al reported retrospectively on 718 women with mixed urinary incontinence who underwent either an autologous rectus fascia pubovaginal sling or a retropubic synthetic midurethral sling. The study reported similar objective cure rates between the 2 groups but higher subjective improvement in the midurethral sling group. Midurethral sling patients also were more than twice as likely to show subjective improvement in UDI-6 and VAS scores than those who underwent fascial slings²¹. Another retrospective study of 242 women who underwent either rectus fascia sling or synthetic midurethral sling reported that women who had an rectus fascia sling “were more likely to report any leakage of urine ($p=.04$) and were 13 times more likely to require urethrolisis ($p<0.001$) than patients with midurethral slings. Fascial sling patients also “reported lower satisfaction (78.5% vs. 92.0%), and had higher rates of urge incontinence (38.0% vs. 25.2%) than did patients who had a midurethral sling.”²²

Few women with urinary incontinence seek medical care for this problem²³. When the morbidity of procedures used prior to TVT is considered, it is not difficult to understand why women might choose to forego treatment for their incontinence altogether, hoping to avoid the complications of invasive surgery and postoperative adverse events associated with the Burch and autologous fascial sling procedures.

Evolution of synthetic materials for treatment of SUI

To avoid the complications associated with harvesting fascia from another site of the body, and in order to attempt to overcome possibly inherent deficiencies of the patient’s own tissue, an effort was made to utilize new materials for suburethral slings. One such material

²¹ Padmanabhan P, et al. Change in urinary storage symptoms following treatment for female stress urinary incontinence. 2016

²² Trabuco EC, et al. Medium-term comparison of continence rates after rectus fascia or midurethral sling placement. Am J Obstet Gynecol 2009 200(3): 300.e1-6

²³ Minassian VA, Yan X, Lichtenfeld MJ, et al. Predictors of care seeking in women with urinary incontinence. Neurourol Urodyn 2012 31(4):470-4

was nylon, but this was associated with infectious risk²⁴. Another material, Mersilene, is a polyester mesh by Ethicon, was widely used in urogynecologic surgery²⁵ but had high levels of tissue rejection requiring surgical excision of many slings. Ultimately, a classification system for mesh used in abdominal surgery helped to identify the best candidates for materials used in suburethral slings. The Amid Type 1 macroporous, monofilament mesh²⁶. These materials, of which polypropylene is an excellent example, allow bacteria into their interstices but also the macrophages that fight infection. They also allow for excellent tissue ingrowth and are inert. Ethicon's Prolene mesh used in TVT and TVT-Exact meets these requirements, and is generally referred to by the medical community and professional societies as an Amid type 1, macroporous, monofilament, lightweight, polypropylene mesh. (AUGS, SUFU 2014 Position Statement on Midurethral Slings). At this time, there is no clinical evidence that another polymer, such as PVDF, would produce the same excellent results in terms of cure rates, patient satisfaction, low complications, and surgeon acceptance, which has been proven time and time again with the TVT and similar polypropylene midurethral slings²⁷. In the current clinical era, surgeons are utilizing synthetic materials to provide a more durable and consistent repair, while reducing the morbidity of an open abdominal incision or need to harvest graft materials. The potential complications of using synthetic grafts for incontinence repairs were commonly known prior the launch of TVT²⁸.

The benefits of TVT revolutionized the treatment of SUI

When the Gynecare TVT by Ethicon was introduced into clinical practice in 1996, the surgical treatment of stress urinary incontinence in women was revolutionized in several ways.

²⁴ Williams TJ, TeLinde RW. The Sling Operation for Urinary Incontinence Using Mersilene Ribbon. *Obstet Gynecol* 1962 19(2): 241-45

²⁵ AM J OBSTET GYNECOL 1995;173;1719-26

²⁶ Amid PK. Classification of biomaterials and their related complications in abdominal wall hernia surgery. *Hernia* (1997) 1:15-21.

²⁷ SCENIHR (Scientific Committee on Emerging and Newly Identified Health Risks), The safety of surgical meshes used in urogynecological surgery, 3 December 2015

²⁸ Iglesia CB, et al. The Use of Mesh in Gynecologic Surgery. In *Urogynecol J* 1997 8:105-15

Not only was its mechanism of action innovative²⁹, but its approach required no abdominal incision, which made it markedly different from its predecessors. Its creators identified Type I polypropylene mesh as superior to materials like Gore Tex and Mersilene³⁰ in terms of improved tissue ingrowth and decreased rejection. The surgical technique of implanting TVT is markedly less invasive than the surgeries for placement of Burch colposuspension or pubovaginal slings. In the procedure, a small 1.5 cm incision is made through the vagina overlying the midurethra, and short dissections are created between this incision and the symphysis pubis on either side of the urethra. The sling is implanted by the passage of thin metal trocars, which can either hug the posterior symphysis pubis and perforate the skin immediately anterior and cephalad to the superior symphysis pubis or traverse the tissues of the obturator foramen. This results in very small, perforate skin incisions in addition to the 1.5 cm vaginal incision. The procedure was initially described to be performed under local anesthetic, and it is an outpatient procedure requiring minimal recovery time. Overall, the patient experience in undergoing surgery for stress incontinence was made far less daunting by the advent of the midurethral sling.

Prior to the pervasive use of the TVT, surgical candidates for the treatment of stress urinary incontinence were offered retropubic procedures, most commonly the Burch urethropexy or a pubovaginal sling. Even after TVT first became available, many practitioners were hesitant to use it, despite its obvious advantages, because they were still awaiting clinical data from a randomized, controlled trial.. This changed when, in 2002, a randomized trial by Ward et al comparing Burch colposuspension to TVT was published. This underpowered equivalence trial showed, using a stringent definition for objective cure, that TVT (66%) was as effective as Burch (57%). While TVT was associated with more intraoperative complications than Burch, primarily in the form of bladder perforation, Burch was associated with more

²⁹ Petros P, Ulmsten U. An integral theory and its method for the diagnosis and management of female urinary incontinence. *Scandinavian Journal of Urology and Nephrology*, Supplement 153, 1993

³⁰ Ulmsten U, et al. An Ambulatory Surgical Procedure Under Local Anesthesia for Treatment of Female Urinary Incontinence. *Int Urogynecol J* 1996; 7:81-86

postoperative complications, more blood loss and OR time, and longer recovery³¹. These data were even more reassuring in light of the ease with which bladder perforations incurred at the time of TVT and recognized intraoperatively could be managed with no clinical sequelae.

After data from a randomized, controlled trial were available to reassure providers of the safety and efficacy of the midurethral sling, it quickly became the surgical treatment of choice for stress incontinence. Additional clinical studies, including more than 100 RCTs firmly established the TVT and synthetic midurethral slings as the first-line treatment of choice for surgical repair of SUI, and as the benchmark procedure against which other devices and procedures would be compared. Hundreds of clinical studies and level 1 RCTs, systematic-reviews and meta-analyses, as well as the overwhelming support and adoption from surgeons and the leading professional societies from around the world, have embraced TVT and the midurethral sling as the gold standard treatment for SUI. Its benefits compared to its predecessor surgeries were so marked that, by the time of my residency training, which began in 2003, the midurethral sling had been embraced as the gold standard, and Burch colposuspensions and fascial slings were reserved for those women who were not candidates for TVT.

As noted by Walters (2012)³², “Almost all surgical procedures for stress urinary incontinence performed today involve placement of a retropubic or transobturator midurethral synthetic sling.” Walters and Weber further describe:

“Although Burch colposuspension and the pubovaginal fascial sling procedures are effective for both primary and recurrent SUI, they are more invasive than midurethral slings, cause more voiding dysfunction, and have significantly longer recovery times, making them less attractive for most primary and recurrent cases of SUI. The evolution of SUI surgeries has shifted so far toward midurethral slings that Burch colposuspension and the pubovaginal sling procedure are rarely performed or taught in obstetrics and gynecology or urology residency programs; these procedures are now mostly done in

³¹ Ward K, Hilton P. Prospective multicenter randomized trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. *BMJ* 2002 325 (7355): 67

³² Walters M, Weber A. Which sling for which SUI Patient? *OBG Management* 2012 24:5, 28-40

fellowship programs by specialists in female pelvic medicine and reconstructive surgery.”

This is consistent with Blaivas (1994), noting that autologous fascial slings never achieved widespread popularity, “primarily due to the perception that the procedure is technically more demanding than the standard urethropexy, and the complication rate, particularly in the hands of the inexperienced surgeon, is reportedly higher.”

Many surveys have demonstrated that Burch colposuspension and fascial sling procedures are no longer commonly performed, and have seen a progressive decline in use since the introduction and rapid adoption of the TVT. In 2002, Davila et al. reported on a survey of International Urogynecological Association (IUGA) members and found that many already considered TVT a procedure of choice for primary management of SUI. The procedures of choice for SUI from this survey were TVT for 48.8% for, Burch for 44%, and autologous fascial slings for 3.8%³³. By 2005, another survey of IUGA members found that the preferred primary incontinence procedure was TVT in 68% of respondents, while the preferred secondary procedure was Burch or transobturator midurethral sling in 13%. Ninety-six percent of respondents were performing TVT. The authors noted that “the predominant surgical procedure of choice is now TVT,” which has “replaced colposuspension as the primary continence surgery of choice.”³⁴ In 2007, a survey of members of the American Urogynecologic Society revealed that 93% of respondents were performing synthetic mesh suburethral slings³⁵.

These shifts were also seen in large database studies. In a 2009 analysis of National Hospital Discharge Survey data, Oliphant, et al. described the decrease in more traditional suburethral sling procedures and retropubic suspension procedures from 1979 to 2004, which was attributed to the increase in the use of midurethral slings replacing these traditional

³³ Davila GW, et al. Pelvic Floor Dysfunction Management Practice Patterns: A Survey of Members of the International Urogynecological Association. *Int Urogynecol J* 2002 13:319-25

³⁴ Jha S, Surgical Management of Stress Urinary Incontinence, A Questionnaire Based Survey. *European Urology* 2005 47:648-52

³⁵ Pulliam SJ, et al. Use of synthetic mesh in pelvic reconstructive surgery: a survey of attitudes and practice patterns of urogynecologists. *Int Urogynecol J* 2007 18:1405-08

procedures³⁶. A review of data from elderly female Medicare beneficiaries with stress incontinence revealed a similar shift to midurethral slings between 1992 and 2001 as the choice for incontinence procedures³⁷. This rapid adoption of midurethral slings and drastic decline in traditional procedures was seen throughout the world. In Taiwan, the time periods from 1997 to 2005 compared to 2006 to 2010 were very different in terms of surgeries performed for stress incontinence in women. There was an increase in midurethral slings from 53.09% to 78.74%, a decrease in Burch from 29.68% to 12.99%, and a decrease in pubovaginal slings declined from 9.33% to 3.46%³⁸.

The shift toward midurethral sling as the first choice surgical procedure for stress incontinence in women affected urologists as well as urogynecologists. Chughtai, et al evaluated incontinence procedures in the United States among ABU urologists from 2003 to 2012, and found that increased midurethral sling usage coincided with a drastic decline in traditional repairs. Of all urologists treating SUI, 93% reported any use of slings, and 53% reported using slings exclusively³⁹. Similarly, Ninety-three percent of urogynecologic surgeons studied in the Value of Urodynamic Evaluation (VALUE) by The Urinary Incontinence Treatment Network study chose to perform a synthetic midurethral sling as the first-line treatment⁴⁰.

Using the 2007 Nationwide Inpatient Sample and the 2006 National Survey of Ambulatory Surgery and applying the US Census Bureau population projections, Wu et al predicted a 47% increase in the number of women who will undergo incontinence surgery, from 210,700 procedures in 2010 to 310,050 procedures in 2050.

³⁶ Oliphant SS, et al. Trends in Stress Urinary Incontinence Inpatient Procedures in the United States, 1979-2004. *Am J Obstet Gynecol* 2009 200(5):521.e1-6

³⁷ Anger JT et al. Trends in surgical management of stress urinary incontinence among female Medicare beneficiaries. *Urology* 2009 74(2):283-7

³⁸ Wu CJ, et al. The surgical trends and time-frame comparison of primary surgery for stress urinary incontinence, 2006-2010 vs 1997-2005. In *Urogynecol J* 2014 25:1683-91

³⁹ Chughtai BI, et al Midurethral Sling Is the Dominant Procedure for Female Stress Urinary Incontinence: Analysis of Case Logs from Certifying American Urologists. *Urology* 2013 82(6):1267-71

⁴⁰ Nager CW, et al. A Randomized Trial of Urodynamic Testing before Stress-Incontinence Surgery. *NEJM* 2012 366:1987-97

TVT is reasonably safe and effective for its intended use of treating SUI

Dyspareunia and chronic pelvic pain are common problems for women in the general population regardless of whether or not they have undergone any type of incontinence procedure. Mathias and Steege conducted a Gallup poll in the U.S. of women aged 18-50 years and found that 14.7% reported having chronic pelvic pain within the past 3 months, and 61% of those with chronic pelvic pain reported that the etiology was unknown⁴¹. Using a questionnaire to evaluate women presenting to primary care settings, Jamieson and Steege reported the high prevalence of dysmenorrhea (90%), dyspareunia (46%), pelvic pain (39%), and Irritable Bowel Syndrome (12%)⁴². Dyspareunia affects up to 22% of women at some point in their lives⁴³. A 1992 national survey of American adults reported that 43% of US women surveyed had sexual dysfunction. The authors noted that sexual dysfunction in women ranges in the literature from 25% to 63%⁴⁴. Later in life, dyspareunia can be a more common problem, regularly affecting up to 40% of postmenopausal women⁴⁵. Reasons for this high rate in older women include physiologic changes to the urogenital tract associated with the menopause.

Dyspareunia and chronic pelvic pain in women are multifactorial, and while any surgery for stress incontinence can contribute to these problems, there are many, many other causes. In Braddom's Physical Medicine and Rehabilitation Textbook, Eickmeyer elucidates the most likely etiologies of pelvic floor pain or dysfunction including vulvodynia, dysmenorrhea, endometriosis, fibroids, pelvic organ prolapse, interstitial cystitis, urgency/frequency syndrome, levator ani syndrome, bowel/bladder incontinence, low back pain, lumbar radiculopathy, sacroiliac joint dysfunction, coccydynia, hip disorders, anxiety, depression, and history of

⁴¹ Mathias SD, et al. Chronic Pelvic Pain: Prevalence, Health-Related Quality of Life, and Economic Correlates. *Obstet Gynecol* 1996 87(3): 321-27

⁴² Jamieson DJ, et al. The Prevalence of Dysmenorrhea, Dyspareunia, Pelvic Pain, and Irritable Bowel Syndrome in Primary Care Practices. *Obstet Gynecol* 1996 87:55-8

⁴³ Steege JF, Zolnoun DA. Evaluation and Treatment of Dyspareunia. *Obstet Gynecol* 2009;113:1124-36

⁴⁴ Laumann EO, et al. Sexual Dysfunction in the United States: Prevalence and Predictors. *JAMA* 1999 281:537-44

⁴⁵ ACOG Practice Bulletin 119, April 2011

abuse.⁴⁶ In a review article, Ferrero et al described causes of deep dyspareunia, including: endometriosis, pelvic congestion syndrome, interstitial cystitis, levator ani muscle myalgia, uterine retroversion, history of sexual abuse, uterine myomas, adenomyosis, pelvic inflammatory disease, ovarian remnant syndrome, and irritable bowel syndrome⁴⁷. Kahn (1997) attributed postoperative dyspareunia to posterior colporrhaphy procedures. Lastly, dyspareunia after pelvic floor repair procedures has been described in the literature for many years⁴⁸.

In women with urinary incontinence, considerations regarding leakage of urine during intercourse may further compromise sexual function. While any vaginal surgery has the potential to cause pain with intercourse, this risk should be weighed against the possible improvement of sexual function that could accompany the treatment of urinary incontinence. The impact of incontinence surgery on sexual function has been well studied. Burch colposuspension and rectus fascia sling both improve sexual function in some women. Overall, however, women evaluated using a validated questionnaire assessing sexual function before and after surgery were found to have worsened sexual function after both procedures⁴⁹. In contrast, likely because of improved continence during intercourse, women undergoing midurethral sling have improved sexual function after surgery⁵⁰.

Complications associated with incontinence surgery include voiding dysfunction, pelvic pain, sexual dysfunction, de novo urgency, and persistent and recurrent incontinence. These are well known to trainees in FPMRS from their first introduction to these procedures. In fact, learning objectives specifically designed for medical students, residents, and fellows specify

⁴⁶ Eickmeyer SM, et al. "Chapter 38: Pelvic Floor Disorders", Braddoms' Physical Medicine and Rehabilitation, 5th Ed. Elsevier, Philadelphia. 2016

⁴⁷ Ferrero S, et al. Deep dyspareunia: causes, treatments, and results. Current Opinion in Obstetrics and Gynecology. 2008 20:394-99

⁴⁸ Francis WJA. Dyspareunia Following Vaginal Operations. Journal of Obstetrics and Gynaecology of the British Commonwealth. 1961 68(1): 1-10

⁴⁹ Cayan F, Dilek S, Akbay E. Sexual function after surgery for stress urinary incontinence: vaginal sling versus Burch colposuspension, Arch Gynecol Obstet (2008) 277:31–36

⁵⁰ Zycynski HM, Rickey L, Dyer KY, et al. Sexual activity and function in women more than 2 years after midurethral sling placement Am J Obstet Gynecol 2012;207:421.e1-6

that these complications can occur and that care for women who undergo surgery for urinary incontinence includes the capacity to manage these complications. Specifically, the American Board of Obstetrics and Gynecology created a Guide to Learning for fellows in FPMRS, and this document delineates the requirement that trainees can describe complications of all procedures to treat stress incontinence, including urethral bulking, retropubic urethropexy, and sling operations. This latter category includes fascial bladder neck slings as well as synthetic midurethral slings.

In addition to thoroughly describing the correct technique for placing midurethral slings, the 2015 Instructions for Use for TVT and TVT Exact describe commonly known complications of incontinence procedures, including the occurrence of acute or chronic pain, urinary urgency or urge incontinence, pain with intercourse, or dyspareunia, and partner discomfort with intercourse (in the event of mesh exposure). Mesh erosion or exposure is commonly referred to as the only unique complication to midurethral slings compared to traditional procedures. The FDA's 2013 Considerations for Surgical Mesh describes how the safety and efficacy of full-length midurethral slings, such as TVT, are well-established in clinical trials. The FDA performed a review of the published literature from 1996 to 2011 and a review of the Medical Device Reports from 2008 to 2011 and described the potential complications that are associated with any incontinence procedure:

“pain, mesh erosion through the vagina (also called exposure, extrusion or protrusion), infection, urinary problems, recurrent incontinence, pain during sexual intercourse (dyspareunia), bleeding, organ perforation, neuro-muscular problems and vaginal scarring. Many of these complications require additional medical intervention, and sometimes require surgical treatment and/or hospitalization. With the exception of mesh erosion, the above complications can occur following a non-mesh surgical repair for SUI.”

This same analysis was similarly stated by the American Urologic Association (AUA) in its 2011 (revised in 2013) position statement on the use of midurethral slings: “Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-

related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well.” The AUA also stated that that “[s]uburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction.”

Surgeon Learning

While the Instructions for Use (IFU) document from Gynecare, the manufacturer of TVT, thoroughly enumerates the potential adverse events associated with the device, most physicians who perform midurethral slings undergo training that exposes them to far more information than is provided in the IFU. (AUA National Medical Student Curriculum; AUGS Resident Learning Objectives; ACGME Program Requirements for Graduate Medical Education in Female Pelvic Medicine and Reconstructive Surgery; ABOG and ABU Guide to Learning in Female Pelvic Medicine and Reconstructive Surgery; IUGA Guidelines for Training in Female Pelvic Medicine and Reconstructive Surgery). For example, in the course of her training, a resident in Urology or Obstetrics and Gynecology will likely see candidates for midurethral sling in the office and learn to counsel them before they go to surgery from their clinical instructors. They will likely see several midurethral slings placed as they receive verbal coaching on the placement technique, and they will themselves place many slings with their own hands. They will then manage these patients in the immediate and delayed postoperative periods and will learn about possible complications and the frequency with which they occur directly through clinical experience, all under the supervision of qualified providers.

The IFU document may serve as a cursory overview of the information they are expected to master, but their training experience will be much broader. Additionally, through continued lifelong self-education and reading, surgeons continue to hone their knowledge. For example, in a follow-up 2 year analysis of a landmark randomized, controlled study known as

the Trial of Midurethral Slings (TOMUS, familiar to most academic urogynecologists, adverse events of transobturator and retropubic midurethral slings were quantified⁵¹. Consistent with other studies, this data reinforced a low bladder perforation rate of 5% with retropubic midurethral slings, a 2-3% mesh exposure rate, and pain lasting longer than 6 month in 2-2.3%. Voiding dysfunction requiring surgery occurred in 3% of women, and milder voiding dysfunction occurred in 2-3.4%. The rectus fascia sling, on the other hand, is associated with a 14% voiding dysfunction rate⁵². De novo urgency incontinence occurs in 0-0.3% of women after midurethral sling (Brubaker et al 2011) and in 3% of women after rectus fascia sling or Burch colposuspension (Albo et al 2007). The 2015 Ford Cochrane Review, 2014 SGS Schimpf Meta-Analysis and Systematic Review, and the AUA's updated 2012 complications appendix all demonstrate lower complications with midurethral slings compared to traditional procedures.

Mesh Properties

Whether the TVT is mechanically cut or laser cut is clinically insignificant and a difference between the two has not been demonstrated by any reliable clinical trials. The Type I polypropylene mesh of which modern synthetic midurethral slings are made is cut sheets into thin strips, which form the slings that are placed with the trocar system included with the devices. The mesh can be cut mechanically or with the use of laser. These two cutting techniques offer different properties to the sling edges, and these properties cause the slings to behave differently when stretched beyond what is expected in clinical use. Ethicon began marketing the TVT using a mechanical cut, similar to how a surgeon would cut or trim mesh in the office, starting in 1997 in Europe, and eventually began offering TVT in a laser cut option in late 2006. Ethicon continues to sell both mechanically cut and laser cut TVT. The initial iteration of Gynecare TVT formed of Prolene mesh cut mechanically, could potentially, if improperly misused or unduly stretched beyond what is expected in clinical use, narrow or lose

⁵¹ Brubaker L, Norton PA, Albo ME, et al. Adverse events over two years after retropubic or transobturator midurethral sling surgery: findings from the Trial of Midurethral Slings (TOMUS) study. *Am J Obstet Gynecol* 2011; 205: 498e1-6

⁵² Albo ME, Richter HE, Brubaker L. Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence. *N Engl J Med* 2007 356(21): 2143-2155

some elements of their architecture near the edges. There is no reliable data showing that this occurs in the clinical setting or that the incidence of complications is causally linked to the mechanically cut nature of the TVT. The TVT Exact, the modern iteration of the TVT synthetic retropubic midurethral sling that became available in 2010, is cut with the use of a laser. It is suggested that slings cut this way are more resistant to the mechanical effects of stretch and maintain their shape if subjected to externally applied longitudinal forces. Despite these differences, mechanically cut TVT slings have not had higher complication rates than those seen with today's laser cut TVT Exact slings. The earliest studies of TVT would have utilized devices created between 1996 and 2007, which would include the patients included in the numerous 10+ year follow-up clinical studies, all of which were exclusively mechanically cut (Olsson 2010⁵³, Groutz 2011⁵⁴, Aigmueller 2011⁵⁵, Heinonen 2012⁵⁶, Serati 2012⁵⁷, Nilsson 2013⁵⁸, Svenningsen 2013⁵⁹, Trabuco 2014⁶⁰).

It is important for surgeons to have options, as some surgeons prefer to use the TVT mechanically cut since that is the device they have consistently used with excellent results and substantial long-term data supporting their safety and efficacy, while other surgeons might appreciate the aesthetic appeal of the sealed edges of the laser cut TVT and TVT-Exact. These early studies involving the TVT mechanically cut mesh revealed time and time again that TVT is safe. The laser cut slings available today are clinically indistinguishable from the mechanically

⁵³ Olsson I, et al. Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence. *Int Urogynecol J*. 2010 21:679-83

⁵⁴ Groutz A, et al. Long-term outcome of transobturator tension-free vaginal tape: efficacy and risk factors for surgical failure. *J Womens Health*. 2011 20(10):1525-28

⁵⁵ Aigmueller T, et al. Ten year follow-up after the tension-free vaginal tape procedure. *Am J Obstet Gynecol*. 2011 205:496

⁵⁶ Heinonen P, et al. Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. *Int J Urol*. 2012 19(11):1003-09

⁵⁷ Serati M et al. Tension-free vaginal tape for the treatment of urodynamic stress incontinence: efficacy and adverse effects at 10-year follow-up. *Eur Urol*. 2012 61:939-46

⁵⁸ Nilsson C et al. Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J*. 2013 19:1043-47

⁵⁹ Svenningsen R. Long-term follow-up of the retropubic tension-free vaginal tape procedure. *Int Urogynecol J*. 2013 24:1271-78

⁶⁰ Trabuco E. Midurethral slings for the treatment of stress urinary incontinence. Long-term follow-up. *Am J Obstet Gynecol*. 2014 123:5 (Suppl)197S.

cut devices. I was trained in the era of the mechanically cut sling, and I can personally attest that today's slings behave identically to those on which I was trained. I have used both mechanically cut and laser cut TVT and have followed my patients closely without any noticeable difference in cure rates, patient satisfaction, or complications. Thubert⁶¹ (2016) compared TVT to TVT-Exact and reported no differences in objective or subjective cure, and complications were similar for the two devices. As such, there is no reliable clinical data to support the theories that mechanically cut TVT has lower complications or mesh exposure or dyspareunia compared to laser cut TVT, and vice versa.

The synthetic midurethral sling is the most well-studied surgical procedure for female stress urinary incontinence. In addition to multiple randomized trials proving its safety and efficacy, there have also been several long-term studies with over 10 years of follow up in women who have undergone this procedure (Nilsson 2008⁶², Aigmueller 2011⁶³, Song 2009⁶⁴). There have also been meta-analyses supporting its use (Ford 2015⁶⁵, Schimpf 2014⁶⁶). Additionally, every major medical society guiding the treatment of stress urinary incontinence in women recommends the synthetic midurethral sling as the gold standard treatment for stress incontinence (Position statements endorsed by and practice guidelines from: AUGS, SUFU, ACOG, AUA, ACOG, SGS, AAGL, IUGA, EAU, NICE).

Even during a time when other surgeries utilizing type 1 polypropylene mesh have been called into questions, the midurethral sling remains the treatment of choice for stress urinary incontinence. For example, in 2011, in a follow up Public Health Notification from one

⁶¹ Thubert T. Bladder injury and success rates following retropubic mid-urethral sling: TVT EXACT™ vs. TVT™. *Eur J Obstet Gynecol Reprod Biol.* 2016 Mar;198:78-83.

⁶² Nilsson, CG. Eleven years prospective follow-up of the TVT procedure for treatment of SUI. *Int Urogyn J.* 2008 19:1043-1047.

⁶³ Aigmueller T. Ten-year follow-up after the TVT procedure. *Am J Obstet Gynecol.* 2011 doi: 10.1016/j.ajog.2011.07.010.

⁶⁴ Song P. The 7-year outcome of tension-free vaginal tape procedure for treating female SUI. *BJUI.* 2009 104, 1113-1117.

⁶⁵ Ford A, et al. Mid-urethral sling operations for stress urinary incontinence in women (review); *The Cochrane Library* 2015, Issue 7.

⁶⁶ Schimpf M, et al. Sling surgery for stress urinary incontinence in women a systematic review and metaanalysis; *Am J Obstet Gynecol* 2014;211:71.e1-27

previously released in 2008, the FDA specified that the risks associated with type 1 polypropylene mesh kits used for the treatment of pelvic organ prolapse were distinctly different from midurethral slings in that complications associated with permanent mesh procedures for pelvic organ prolapse were not rare, and these procedures did not improve outcomes compared with other, more traditional procedures. The practice pattern of implanting predominately synthetic midurethral slings also did not change or decrease after the FDA's 2011 Public Health Notice⁶⁷. Furthermore, in a joint statement by the AUGS and IUGA, the safety and efficacy of the synthetic midurethral sling was asserted, and the difference in risk associated with midurethral sling compared with mesh procedures for pelvic organ prolapse was emphasized.

Professor Ulmsten, the inventor of the TVT, passed away in 2004 as a well-respected surgeon (Dwyer 2004⁶⁸; Nilsson 2015⁶⁹; Petros 2015⁷⁰). I am aware that Professor Ulmsten had a potential conflict of interest given his royalties and fees collected from Ethicon/Gynecare; however, Professor Ulmsten's clinical results have been replicated time and time again in a variety of patient types and by surgeons all over the world with differing levels of surgical experience. Every major medical society continues to endorse and advocate for the use of midurethral sling, including the TVT, as the gold standard or first-line treatment option for uncomplicated SUI.

The Prolene mesh used in TVT incites a minimal foreign body reaction (Falconer, 2001⁷¹). A pathological chronic inflammatory response does not correlate with chronic pain

⁶⁷ Clemons JL. Impact of the 2011 FDA transvaginal mesh safety update on AUGS members' use of synthetic mesh and biologic grafts in pelvic reconstructive surgery. *Female Pelvic Med Reconstr Surg* 2013 19(4):191-8

⁶⁸ Dwyer P. Ulf Ulmsten (1938-2004) leader and innovator in urogynaecology. *Int. Urogyn J.* 2004 15:221-222.

⁶⁹ Nilsson CG. Creating a gold standard surgical procedure: the development and implementation of TVT: Ulf Ulmsten Memorial Lecture 2014. *Int Urogynecol J.* 2015 Jun;26(6):787-9.

⁷⁰ Petros P. Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. *Int Urogynecol J.* 2015 Apr;26(4):471-6.

⁷¹ Falconer C, et al. Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. *Int Urogyn J*, 2001 (Suppl 2): S19-S23.

(Hill, 2015⁷²). TVT is made from the same Prolene polypropylene fibers as Prolene sutures, which have demonstrated an excellent safety profile since being approved as a New Drug Application by the FDA in the late 1960s. TVT has one of the largest pore sizes available for slings on the market in the United States at 1,379 microns or 1 millimeter (Moalli, 2008⁷³). Although some of the hernia literature refers to large, flat sheets of polypropylene mesh as “heavyweight,” the TVT sling is considered by urogynecologists to be a smaller mesh load given the small 1cm wide surface area and large pores (substantially larger than Amid’s 75 micron requirement for macroporous meshes). There is no reliable clinical evidence to support plaintiffs’ experts’ theories that the TVT pores are too small, it degrades over time, causes chronic foreign body reactions, fibrotic bridging, mesh contracture/shrinkage, fraying, particle loss, biofilm formation and infections, has sharp edges, ropes, curls and deforms, or that the pores collapse with tension. These opinions are primarily based on company emails and documents taken out of context, and not on reliable clinical evidence. Nor are these opinions consistent with my clinical experience, review of the medical literature, and discussions with colleagues.

There is no reliable clinical evidence that TVT degrades in vivo. Ethicon’s 7 year dog study evaluating Prolene sutures did show some “cracking” under SEM; however, the report found that there was no degradation as there was no significant change in molecular weight or tensile strength. Thames⁷⁴ et al (2016) concluded after extensive testing on Ethicon’s Prolene meshes that the “cracking” that has been described in some studies is not the degraded polymer, but rather, an out coating that forms during the formalin fixation process. They concluded that: “Our effective cleaning of explanted Prolene meshes and subsequent analyses showed that they did not degrade in vivo, confirming the in vivo stability of properly formulated polypropylene. Instead, the cracked layer that some researchers have identified as degraded

⁷² Hill A, Unger C, Solomon E, Brainard J, Barber M. Histopathology of excised midurethral sling mesh. *Int Urogyn J*, 2015 26:591-595.

⁷³ Moalli P, et al. Tensile properties of five commonly used mid-urethral slings relative to TVT. *Int Urogyn J*, 2008; 19:655-663

⁷⁴ Thames S, et al. The myth: in vivo degradation of polypropylene-based meshes. *Int Urogyn J*, 2016.

Prolene is an adsorbed protein–formaldehyde coating, resulting from the well-established formalin–protein fixation process, which occurs immediately upon placing an explant in formalin.”

TVT is described as a tension-free procedure, primarily because it is placed with a spacer and without tension, and is fixed into place by friction and tissue integration rather than sutures. The clinical data does not support the theory that TVT undergoes any clinically relevant shrinkage or contraction in vivo, which has been confirmed by ultrasound studies and long-term evaluation (Lo, 2004⁷⁵; Dietz, 2003⁷⁶; Nilsson, 2013⁷⁷). If TVT did undergo clinically significant shrinkage, then the urinary retention rates would be drastically higher than they are shortly after the procedure, which is not the case for TVT in the short-term or long-term. Surgeons gain experience using surgeon judgment as to properly place and adjust the tension of TVT, similar to how surgical judgment is required to place the tension on an autologous fascial sling or the sutures in a Burch procedure.

There is no reliable clinical evidence that TVT is carcinogenic or causes cancer. Similarly, there is little to no clinical relevance of a Material Safety Data Sheet as a concern related to potential oxidation/degradation – as demonstrated above by Thames (2016) – or related to the carcinogenic or cytotoxic potential (King, 2014⁷⁸; Moalli, 2014⁷⁹; Linder, 2016⁸⁰). Moalli (2014) discussed the dangers of giving credence to the suggestion that the MSDS for raw material polypropylene pellets is of any clinical significance: “As we learned from the silicone breast implant controversy several decades ago, publications derived from a skewed interpretation of

⁷⁵ Lo TS, et al. Ultrasound assessment of mid-urethra tape at three-year follow-up after tension-free vaginal tape procedure. *Urology*. 2004 Apr;63(4):671-5.

⁷⁶ Dietz HP, et al. Does the tension-free vaginal tape stay where you put it? *Am J Obstet Gynecol*. 2003 Apr;188(4):950-3.

⁷⁷ Nilsson CG, et al. Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. *Int Urogynecol J*. 2013 Aug;24(8):1265-9.

⁷⁸ King A. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. *Curr Urol Rep*. 2014 15:453.

⁷⁹ Moalli P. Polypropylene mesh: evidence for lack of carcinogenicity. *Int Urogyn J*. 2014 25:573-576.

⁸⁰ Linder B. Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. *Int Urogyn J*. 2016 27:1333-1336.

the literature and not solid evidence based on scientific data can lead to baseless damaging media hype and unscrupulous jury awards. It would be a tragedy for women worldwide if non-scientifically based articles regarding the potential hazards of polypropylene incited a spiraling course for the best (highest success rate and minimal morbidity) surgical procedure developed to date for stress urinary incontinence simply because of liability concerns by doctors, hospitals, and manufacturers. As treating physicians, we must let science and clinical studies determine our practice. More importantly, we must align with the millions of women who have been successfully treated with mesh with absolutely no evidence of systemic complications (including cancer) and who have regained control of their quality of life.⁸¹”

There is no reliable clinical evidence demonstrating a superior safety and efficacy profile of a lighter weight, larger pore, laser cut mesh as compared to TVT. Substantial RCTs would be necessary to substantiate such a claim.

In conclusion, the TVT, both mechanically cut and laser cut, and TVT-Exact are state of the art Amid type 1, macroporous, monofilament, lightweight, polypropylene midurethral slings which have been studied and evaluated more than any other device or procedure to treat incontinence, and are considered the standard of care for the primary treatment of SUI. The benefits of TVT and synthetic midurethral slings far outweigh those of the more invasive traditional procedures, even considering the potential 1-3% risk of mesh exposure or erosion. As such, there is no alternative design that would produce the same high objective cure rates while eliminating the well-known potential complications reported in the TVT literature.

⁸¹ Moalli P, et al. Polypropylene mesh: evidence for lack of carcinogenicity. *Int Urogynecol J* 2014 25:573-76

Signed: 

Date: January 30, 2017